MMACHC gene

methylmalonic aciduria (cobalamin deficiency) cblC type, with homocystinuria

Normal Function

The *MMACHC* gene provides instructions for making a protein that helps convert vitamin B12 (also called cobalamin) into one of two molecules, adenosylcobalamin (AdoCbl) or methylcobalamin (MeCbl). AdoCbl is required for the normal function of an enzyme known as methylmalonyl CoA mutase. This enzyme helps break down certain protein building blocks (amino acids), fats (lipids), and cholesterol. AdoCbl is called a cofactor because it helps methylmalonyl CoA mutase carry out its function. MeCbl is also a cofactor, but for an enzyme known as methionine synthase. This enzyme converts the amino acid homocysteine to another amino acid, methionine. The body uses methionine to make proteins and other important compounds.

Research indicates that the MMACHC protein plays a role in processing different forms of vitamin B12 so that they can be converted to either of the cofactors, AdoCbl or MeCbl. MMACHC also interacts with another protein called MMADHC (produced from the *MMADHC* gene). Together these proteins transport the processed vitamin B12 to regions of the cell in which each cofactor is needed: specialized structures that serve as energy-producing centers (the mitochondria), where AdoCbl functions, or the fluid inside the cell (the cytoplasm), where MeCbl functions. Additional chemical reactions then convert vitamin B12 into AdoCbl or MeCbl.

Health Conditions Related to Genetic Changes

methylmalonic acidemia with homocystinuria

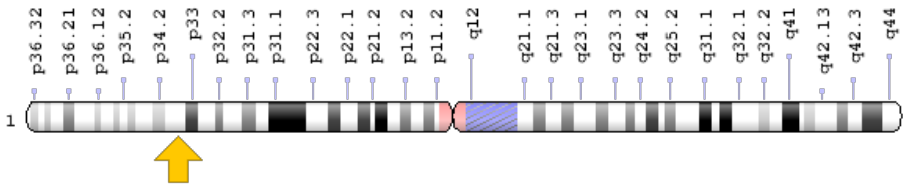
Dozens of *MMACHC* gene mutations have been found to cause methylmalonic acidemia with homocystinuria, cblC type, the most common form of a disorder that causes developmental delay, eye defects, neurological problems, and blood abnormalities. The most common mutation involved in this condition, called 271dupA, inserts an extra DNA building block (nucleotide) at position 271 of the gene. This change alters the protein blueprint, leading to production of an abnormally short protein that is unable to function. Other *MMACHC* gene mutations also lead to production of a protein with impaired function. A shortage of functional MMACHC protein prevents normal processing and transport of vitamin B12, impairing production of both AdoCbl and MeCbl. Because both of these cofactors are missing, the enzymes that require them (methylmalonyl CoA mutase and methionine synthase) do not function normally. As a result, certain amino acids, lipids, and cholesterol are not broken down and homocysteine cannot be converted

to methionine. This dual defect results in a buildup of toxic compounds as well as homocysteine, and a decrease in the production of methionine within the body. This combination of imbalances leads to the signs and symptoms of methylmalonic acidemia with homocystinuria.

Chromosomal Location

Cytogenetic Location: 1p34.1, which is the short (p) arm of chromosome 1 at position 34.1

Molecular Location: base pairs 45,500,184 to 45,511,266 on chromosome 1 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- cblC
- DKFZP564I122
- methylmalonic aciduria and homocystinuria type C protein

Additional Information & Resources

GeneReviews

- Disorders of Intracellular Cobalamin Metabolism
  https://www.ncbi.nlm.nih.gov/books/NBK1328

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28MMACHC%5BTIAB%5D%29+OR+%28methylmalonic+aciduria+++cblC+type,+with+homocystinuria%5BTIAB%5D%29%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D

OMIM

- MMACHC GENE
  http://omim.org/entry/609831

Research Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology
  http://atlasgeneticsoncology.org/Genes/GC_MMACHC.html
- ClinVar
  https://www.ncbi.nlm.nih.gov/clinvar?term=MMACHC%5Bgene%5D
- HGNC Gene Symbol Report
  http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=24525
- NCBI Gene
  https://www.ncbi.nlm.nih.gov/gene/25974
- UniProt
  http://www.uniprot.org/uniprot/Q9Y4U1

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